

Seroepidemiology of vaccine-preventable and emerging RNA viruses in Rwanda

Akademisk avhandling

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Avhandlingen baseras på följande delarbeten

- I. **Seruyange E.**, Gahutu J.B., Muvunyi M.C., Zena Uwimana G., Gatera M., Twagirumugabe T., Swaibu K., Karenzi B., Bergström T. Measles seroprevalence, outbreaks and vaccine coverage in Rwanda. *Infectious Diseases 2016*, 48:11-12, 800-807
- II. **Seruyange E**, Gahutu JB, Muvunyi CM, Katare S, Ndahindwa V, Sibomana H, Nyamusore J, Rutagarama F, Hannoun C, Norder H, Bergström T. Seroprevalence of Zika virus and Rubella virus IgG among blood donors in Rwanda and in Sweden. *J Med Virol*. 2018; 90:1290–1296
- III. **Seruyange Eric**, Karl Ljungberg, Claude Mambo Muvunyi, Jean Bosco Gahutu, Swaibu Katare, José Nyamusore, Helene Norder, Peter Liljeström, Tomas Bergström. High seroprevalence of Chikungunya Virus IgG in Rwandan blood donors. *Vector-Borne and Zoonotic Diseases*, 2018. *Under revision*
- IV. **Seruyange E**, Bergström T. Linear Epitope Analysis of Sera from Rwandan and Swedish Blood Donors with dual seroreactivity to West Nile and Tick-borne Encephalitis viruses. *Preliminary manuscript*, 2018

**SAHLGRENKA AKADEMIN
INSTITUTIONEN FÖR BIOMEDICIN**



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Abstract

Infectious diseases are a leading cause of death in sub-Saharan Africa, and in Rwanda diarrhea, lower respiratory and other common infections are linked to high mortality and morbidity. For children <5 years of age, neonatal/congenital disorders rank second among causes of death in Rwanda. However, neither the burden of, nor immunity to, fever-causing viruses in children and adults are currently known.

Despite recent progress of vaccination in Rwanda, childhood infections including measles are regularly reported to WHO. To assess immunity to vaccine-preventable viruses, and susceptibility to emerging arboviruses, we investigated the seroprevalence by ELISA of IgG to MeV, RuV, ZIKV, CHIKV, and WNV on samples from Rwandan and Swedish blood donors collected during 2015 for comparative studies.

The seroprevalence of MeV in Rwandan blood donors was low (71.5%) compared to that in Swedish donors (92.6%). This might be related to the previous one dose measles vaccine policy in Rwanda, (two doses were introduced in 2014). Yet, a comparably high seroprevalence was observed in older Rwandan and Swedish donors (90.4% versus 94.1%). The measles outbreak in Rwanda, 2010-2011, was investigated by PCR; sequencing revealed that these outbreak strains belonged to genotype B3, and were related to measles strains from neighboring countries.

Rwandan blood donors were also tested for IgG to ZIKV and RuV, both viruses that can cause congenital infections. The ZIKV assay showed a seropositivity rate of 1.4%, and all 12 samples that were positive for anti-ZIKV IgG antibodies were negative by RT-PCR, arguing against active infection. Almost all women of childbearing age were found to be susceptible to ZIKV. In addition, a larger proportion of Rwandan women of childbearing age were seronegative for RuV (10.5%) compared to males (6.5%).

Among Rwandan donors, anti-CHIKV IgG and anti-WNV IgG antibodies were detected at the rates of 63% and 10.4%, respectively. The highest seroprevalence for both viruses was recorded within the Eastern Province, with 86.7% and 33.3% for CHIKV and WNV IgG, respectively. Both *Culex* and *Aedes* mosquitos were most prevalent in the Eastern Province. Swedish blood donors, as expected, showed a much lower seroprevalence for CHIKV, 8.5%. Surprisingly, the seroprevalence for WNV in Swedish donors was relatively high, 14.1%. This stimulated investigation for possible serological cross-reactivity with another flavivirus circulating in Sweden, i.e. TBEV. Dual seroreactivities of 78.6% and 70.3% were observed to WNV and TBEV in Swedish and in Rwandan donors, respectively. Furthermore, 19 of the 28 Swedish sera seropositive to WNV were confirmed by plaque reduction neutralization test as being anti-TBEV IgG antibody-positive, with possible cross-reactivity to WNV.

This dual seroreactivity to WNV and TBEV, seen in samples from both countries, was further characterized on pepscan analyses of E protein linear epitopes. Although we could define several novel IgG epitopes of both viruses, we found no explanation of their serological cross-reactivity. Instead, this phenomenon could be related to reactivity to discontinuous epitopes, or to IgG directed to flaviviral proteins other than the E protein. Surprisingly, the strongest peptide responses detected were from a pool of Rwandan plasma samples that reacted to linear epitopes of the E-protein of TBEV rather than WNV. This finding suggests the circulation of hitherto undiscovered tick-borne flaviviruses in Rwanda, which may share conserved epitopes with TBEV.

Keywords: Seroprevalence, measles virus, rubella virus, Zika virus, West Nile virus, chikungunya virus, tick-borne encephalitis virus, mosquitoes, linear epitopes, Rwanda, Sweden